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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,344	06/25/2003	Tuo Jin	692-A-US	3985

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EXAMINER
ALSTRUM ACEVEDO, JAMES HENRY

ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,344	JIN, TUO	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-38* is/are pending in the application.

4a) Of the above claim(s) *33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-32 and 35-38* is/are rejected.

7)☒ Claim(s) *20, 23, 24, 26, and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 20-38 are pending. Applicants have cancelled all the original claims (i.e. claims 1-19). Claims 20-38 are new. Receipt and consideration of Applicant's amended claim set and arguments/remarks submitted on December 19, 2006 and is acknowledged. Claims 33-34 are withdrawn from consideration as being drawn to a non-elected invention (see restriction requirement mailed June 14, 2006 and made final in the office action mailed on September 19, 2006). **Claims 20-32 and 35-38 are under consideration in the instant office action.**

Moot Rejections/objections

All rejections and/or objections of claims 1-19 cited in the previous office action mailed on September 19, 2006 **are moot**, because said claims have been cancelled.

Specification

The objection to the disclosure because of the informalities set forth on page 3 of the office action mailed on September 19, 2006 **is withdrawn** per Applicant's amendments correcting said informalities.

Claims 20, 23, 24, 26, and 31 are objected to because of the following informalities: (1) the word "of" should be inserted in claim 20, line 2, after the word, "consisting"; (2) a comma should be inserted in claim 23, line 3 after the word "microemulsion;" (3) on line 1 of claim 24 it appears that either the word "said" or the article "the" is erroneously present; (4) the words "gelucire" and "bay" in claim 26 are not proper nouns and should not be capitalized; (5)

the word "triamterene" is misspelled in claim 31, line 2 as "triamteren". Appropriate correction is required.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 20-28, 31-32, and 35-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Pather et al. (U.S. Patent No. 6,280,770; IDS reference) as evidenced by K. Y. Yang et al. ("Effects of Amorphous Silicon Dioxides on Drug Dissolution," *Journal of Pharmaceutical Sciences*, 1979, *68(5)*, 560-565).

Applicant claims a composition in the form of a free flowing compressible powder consisting of (claim 20 only) or comprising porous particles and solid lipids that are absorbed in the pores of the particles.

NOTE: Claims 35-38 are product-by-process claims. Process steps that do not modify the structural characteristics of the instant products are given no weight, as is the case for claims 35-38 of the instant application (MPEP §2113).

Pather discloses microemulsion as solid dosage forms for oral administration comprising drug-containing microemulsions absorbed onto solid particles, which may be further formulated into solid dosage forms, and improve the bioavailability of a wide range of drugs (title, abstract, Fig. 1). Microemulsions are pharmaceutically acceptable carriers. The bioavailability of a drug (i.e. its absorption after administration) is attributed to two processes: (1) dissolution of the drug in physiological fluids and (2) the absorption process itself (col. 1, lines 34-37). Specifically, Pather discloses pharmaceutical carrier microemulsions, which are absorbed onto solid particulate absorbents (col. 4, lines 25-29), which can be combined with additional excipients and made into other solid dosage forms, including **tablets, granules, pellets, or other multiparticulate, capsules, and free-flowing powders** (col. 6, lines 8-10, 64-67; col. 9, lines 23-33 [tablets], 34-48 [coated tablets], 49-56 [pellets], 58-67 and col. 10, lines 1-2 [granules]; Examples 1-4, claims 10-16). In Pather's compositions, the drugs are maintained in a microemulsion in vivo, which thereby **enhances dissolution** (col. 3, lines 12-18 and 22-25).

Pather discloses that any non-toxic oil may be used including, **mono-, di-, and triglycerides, *fatty acids* and their esters**, esters of propylene glycols or other polyols, natural oils, such as cottonseed oil, soybean oil, sunflower oil, canola oil, etc. (col. 5, lines 35-43). Any non-toxic surfactant may be used in the microemulsion including various grades of commercial products: TWEENS® (polyethylene glycol sorbitan laurates), ARLACEL® (dianhydro-d-

mannitol monooleate), CAPMUL® (mono-and diglycerides of glycerine and specific fatty acids), MIGLYOL® (coconut oil triglycerides), etc. (col. 5, lines 35-44). The non-toxic absorbent is preferably a fine particulate, including clays, **silicon dioxide (i.e. silica),** wherein silica is preferred (col. 5, line 66 though col. 6, line 7; claim 6). Examples of drugs suitable for incorporation into Pather's invented compositions include **acyclovir, doxepin, doxorubicin, labetalol, methyldopa, nalbuphine, pentoxifyll, and cyclosporin** (col. 6, lines 57-63; claim 10). Examples of filler excipients (i.e. diluents) that can be used to make a tablet from Pather's compositions include mannitol, dextrose, sucrose, and calcium carbonate (col. 9, lines 42-43).

Pather lacks the express disclosure that the invented compositions are capable of absorbing a lipid in the melt state. It is the Examiner's position that this property is inherent to silicon dioxide (i.e. silica), because this is the same material claimed by Applicant as having said property. Because Pather's compositions comprise silica as an absorbent material these compositions inherently have the property of absorbing a lipid in the melt state. Dependent claim 28 requires that the powders have a surface area greater than 100 m^2/g. It is Examiner's position that the silica used by Pather is inherently porous and has a surface area greater than 100 m^2/g as evidenced by Table I in Yang et al. (pg. 561) where it is demonstrated that several commercially available amorphous silicon dioxides (i.e. silicas) all have surface areas of 290 m^2/g or more and porous structures, as evidenced by the fact that all three silicas in Table I have measurable average pore diameters.

Response to Arguments

Applicant's arguments filed December 19, 2006 have been fully considered but they are not persuasive. Applicant's traversal arguments of the instant rejection are based on (1) Applicant's disagreement that the property of absorbing lipids in the melt state is inherent to silicon dioxide; (2) Applicant's claimed method does not require pre-formulation of an emulsion, such as was reported by Pather and Yang; and (3) according to Exhibit A, Applicant's method results in different compositions than those disclosed by Pather. The Examiner respectfully disagrees with Applicant's traversal arguments. Regarding Exhibit A, it is noted that extraneous evidence not already provided in the specification must be submitted in declaration form (see MPEP § 716 and 37 C.F.R. 1.132). Exhibit A represents extraneous evidence not disclosed in the instant specification and this evidence has not been properly submitted in declaration format. As a result, the evidence in Exhibit A has not been considered. Even if the alleged "evidence" in Exhibit A were properly submitted in declaration format, it would not be persuasive, because it merely represents a cartoon depiction of Applicant's opinion concerning Applicant's perceived differences between the claimed composition and Pather's disclosed composition. Applicant's exhibit contains no data comparing the two compositions that demonstrates that Pather's compositions do not inherently exhibit the property of absorbing lipids in the melt state. Traversal argument (2) is unpersuasive, because the claims under consideration are compositions not methods. Furthermore, regarding the product-by-process claims, the differences between the methods disclosed by Applicant and Pather's method are immaterial to patentability, because these procedural differences do not result in structural modifications of the claimed compositions. Therefore, this instant rejection as applied to the new claims, remains proper.

Claims 20, 22, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by A. Sheth et al. ("Use of Powdered Solutions to Improve the Dissolution Rate of Polythiazide Tablets," *Drug Development and Industrial Pharmacy*, 1990, *16(5)*, 769-777 [IDS reference]) as evidenced by K. Y. Yang et al. ("Effects of Amorphous Silicon Dioxides on Drug Dissolution," *Journal of Pharmaceutical Sciences*, 1979, *68(5)*, 560-565).

Applicant's claims have been described above.

Sheth discloses **free-flowing powder (i.e. granular) compositions compressed into tablet formulations** by direct compression and comprising solutions of polythiazide (a drug) in polyethylene glycol 400 in admixture with microcrystalline **cellulose** (RC-591) and silica, wherein the **dissolution rate of polythiazide from these tablets was significantly more rapid than from commercially available tablets**. The silica utilized by Sheth is characterized as having a large surface area, **high porosity**, and unique absorption properties (pg. 770, 4th paragraph and pg. 771, Materials section). Sheth concluded that the dissolution rate of sparingly soluble, hydrophobic drugs can be markedly improved by incorporation of powdered solution into tablets (conclusion #1) (abstract; "Preparation of Powdered Solution of Polythiazide" pg. 771-772; "Preparation of Tablets" on page 772; Figure. 1 on pg. 774 and paragraph on said page; conclusions on pg. 776-777).

Response to Arguments

Applicant's arguments filed December 19, 2006 have been fully considered but they are not persuasive. Applicant's traversal argument of the instant rejection is based on Applicant's disagreement that the property of absorbing lipids in the melt state is inherent to silicon dioxide.

Applicant has provided no evidence to demonstrate that this property is not inherent to the composition disclosed by Sheth. This rejection remains proper.

Claims 20, 22, and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by K. Y. Yang et al. ("Effects of Amorphous Silicon Dioxides on Drug Dissolution," *Journal of Pharmaceutical Sciences*, 1979, *68(5)*, 560-565).

Applicant's claims have been described above.

Yang discloses the effects of amorphous silicon dioxides (i.e. silicas) on drug dissolution (title, abstract, Fig. 1, Fig. 2, Tables III-VI, Fig. 4). In most of the samples studied the incorporation of amorphous silica greatly enhanced the amount of drug dissolved, regardless of the silica sample used, with the exception of prednisone-silica 63 depicted in Fig. 2. The drugs studied were digoxin, griseofulvin, and prednisone, which are hydrophobic drugs that are either water insoluble or poorly water-soluble.

Yang (pg. 561) demonstrated that the commercially available amorphous silicon dioxides (i.e. silicas) used in the study all have surface areas of 290 m^2/g or more; and porous structures, as evidenced by the fact that all three silicas in Table I have measurable average pore diameters. Silica 63, silica 72, and silica 266 have pore diameters of 20 Å, 150 Å, and 210 Å, which meets the limitation of claim 29 for all silicas used by Yang (1 Å = 0.1 nm).

Response to Arguments

Applicant's arguments filed December 19, 2006 have been fully considered but they are not persuasive. Applicant's traversal arguments of the instant rejection are the same as those

discussed above in the instant office action in the rejections under 35 U.S.C. § 102(b) and 102(e). The Examiner's position regarding these traversal arguments applied to the instant rejection is the same as stated above in the instant office action. The instant rejection remains proper.

Conclusion

Claims 20-32 and 35-38 are rejected. Claims 20, 23, 24, 26, and 31 are objected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571)

272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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